continuation-in-part of U.S. Application No. 08/176,427, filed December 30, 1993, the teachings of which are incorporated herein by reference.

Please replace the partial paragraph at the top of page 14 with the following:

introns interrupting the Drosophila *hh* and M-*Dhh* open reading frames are indicated by arrowheads. All amino acids shared among the six predicted *hh* proteins are indicated in bold. Figure 5B is a sequence alignment of the N-terminal portion of vertebrate *hedgehog* proteins (mDhh (SEQ ID No. 9, residues 23-189), mIhh (SEQ ID No. 10, residues 76-193), hIhh (SEQ ID No. 14, residues 1-94), hShh (SEQ ID No. 13, residues 24-188), cShh (SEQ ID No. 8, residues 27-191), mShh (SEQ ID No. 11, residues 25-189), zShh (SEQ ID No. 12, residues 24-188)), and the predicted degenerate sequence "CON" (SEQ ID No: 41).

Please replace the last full paragraph on page 14 and the paragraph bridging pages 14 and 15 with:

Figures 9A and 9B illustrate the comparison of zebrafish *Shh* (Z-*Shh*) (SEQ ID No. 12, residues 1-415) and Drosophila *hh* (hh) (SEQ ID No. 34) amino acid sequences. Figure 9A is an alignment of zebrafish *Shh* and Drosophila *hh* amino acid sequences. Identical amino acids are linked by vertical bars. Dots indicate gaps introduced for optimal alignment. Putative transmembrane/signal peptide sequences are underlined (Kyte and Doolittle (1982) *J Mol Biol* 157:133-148). The position of exon boundaries in the Drosophila gene are indicated by arrowheads. The region of highest similarity between Z-*Shh* and *hh* overlaps exon 2. Figure 9B is a schematic comparison of Z-*Shh* and drosophila *hh*. Black boxes indicate the position of the putative transmembrane/signal peptide sequences. relative to the amino-terminus. Sequence homologies were scored by taking into account the alignment of chemically similar amino acids and percentage of homology in the boxed regions is indicated.

Figure 10 is an alignment of partial predicted amino acid sequences from three different zebrafish *hh* homologs and Drosophila *hh* (SEQ ID No. 34). One of these sequences

corresponds to *Shh* (SEQ ID No. 12), while the other two define additional *hh* homologs in zebrafish, named *hh*(a) (SEQ ID No. 16) and *hh*(b) (SEQ ID No. 17). Amino acid identities among the three partial homologs are indicated by vertical bars.

Please replace the last paragraph on page 142 with:

Various fragments of the mouse *Shh* gene were cloned into the pET11D vector as fusion proteins with a poly(His) leader sequence to facilitate purification. Briefly, fusion genes encoding the mature M-*Shh* protein (corresponding to Cys-25 through Ser-437 of SEQ ID No. 11) or N-terminal containing fragments, and an N-terminal exogenous leader having the sequence M-G-S-S-H-H-H-H-H-H-L-V-P-R-G-S-H-M (SEQ ID No. 47) were cloned in pET11D and introduced into *E. coli*. The poly(His)-*Shh* fusion proteins were purified using nickel chelate chromatography according to the vendor's instructions (Qiagen catalog 30210), and the poly(His) leader cleaved from the purified proteins by treatment with thrombin.

The replacement paragraphs presented above incorporate changes as indicated by the marked-up versions below.

This application is a continuation of U.S. Application No. 08/462,386, filed June 5, 1995, which is a continuation-in-part of U.S.[S.N. Serial] Application No. 08/435,093, filed May 4, 1995, which is a continuation-in-part of U.S.[S.N. Serial] Application No. 08/356,060, filed December 14, 1994, which is a continuation-in-part of U.S.[S.N. Serial] Application No. 08/[227,371]176,427, filed December 30, 1993 [and entitled "*Vertebrate Embryonic Pattern-Inducing Proteins and Uses Related Thereto*"], the teachings of which are incorporated herein by reference.

introns interrupting the Drosophila *hh* and M-*Dhh* open reading frames are indicated by arrowheads. All amino acids shared among the six predicted *hh* proteins are indicated in bold.

Figure 5B is a sequence alignment of the N-terminal portion of vertebrate *hedgehog* proteins (mDhh (SEQ ID No. 9, residues 23-189), mIhh (SEQ ID No. 10, residues 76-193), hIhh (SEQ ID No. 14, residues 1-94), hShh (SEQ ID No. 13, residues 24-188), cShh (SEQ ID No. 8, residues 27-191), mShh (SEQ ID No. 11, residues 25-189), zShh (SEQ ID No. 12, residues 24-188)), and the predicted degenerate sequence "CON" (SEQ ID No: 41).

Figures 9A and 9B illustrate the comparison of zebrafish *Shh* (Z-*Shh*) (SEQ ID No. 12, residues 1-415) and Drosophila *hh* (hh) (SEQ ID No. 34) amino acid sequences. Figure 9A is an alignment of zebrafish *Shh* and Drosophila *hh* amino acid sequences. Identical amino acids are linked by vertical bars. Dots indicate gaps introduced for optimal alignment. Putative transmembrane/signal peptide sequences are underlined (Kyte and Doolittle (1982) *J Mol Biol* 157:133-148). The position of exon boundaries in the Drosophila gene are indicated by arrowheads. The region of highest similarity between Z-*Shh* and *hh* overlaps exon 2. Figure 9B is a schematic comparison of Z-*Shh* and drosophila *hh*. Black boxes indicate the position of the putative transmembrane/signal peptide sequences. relative to the amino-terminus. Sequence homologies were scored by taking into account the alignment of chemically similar amino acids and percentage of homology in the boxed regions is indicated.

Figure 10 is an alignment of partial predicted amino acid sequences from three different zebrafish *hh* homologs and Drosophila *hh* (SEQ ID No. 34). One of these sequences corresponds to *Shh* (SEQ ID No. 12), while the other two define additional *hh* homologs in zebrafish, named *hh*(a) (SEQ ID No. 16) and *hh*(b) (SEQ ID No. 17). Amino acid identities among the three partial homologs are indicated by vertical bars.

Various fragments of the mouse *Shh* gene were cloned into the pET11D vector as fusion proteins with a poly(His) leader sequence to facilitate purification. Briefly, fusion genes encoding the mature M-*Shh* protein (corresponding to Cys-25 through Ser-437 of SEQ ID No. 11) or N-terminal containing fragments, and an N-terminal exogenous leader having the sequence M-G-S-S-H-H-H-H-H-H-L-V-P-R-G-S-H-M (SEQ ID No. 47) were cloned in pET11D and introduced into *E. coli*. The poly(His)-*Shh* fusion proteins were purified using nickel chelate chromatography according to the vendor's instructions (Qiagen catalog 30210), and the poly(His) leader cleaved from the purified proteins by treatment with thrombin.

In the claims:

For the convenience of the Examiner, all claims being examined, whether or not amended, are presented below.

Please cancel claim 81 without prejudice.

1. (Amended) A method for promoting one or more of growth, differentiation, and survival of neuronal cells, comprising contacting said cells with an [effective] amount of a *hedgehog* polypeptide at least 80% identical to a sequence selected from SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID No: 20, SEQ ID NO: 21 and N-terminal fragments of the preceding sequences that bind to a naturally occurring *patched* receptor, wherein the amount of the *hedgehog* polypeptide is effective to promote one or more of growth, differentiation, and survival of said cells.

49. (Amended) A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells with an effective amount of a *hedgehog* polypeptide at least 80% identical to a sequence selected from SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID No: 20, SEQ ID NO: 21 and N-terminal fragments of the preceding sequences that bind to a naturally occurring *patched* receptor, thereby increasing the [rate of] survival rate of the neuronal cells.

50. (Amended) A method for promoting growth of mammalian neuronal stem cells, comprising treating the cells with an [effective] amount of a *hedgehog* polypeptide at least 80% identical to a sequence selected from SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID No: 20, SEQ ID NO: 21 and N-terminal fragments of the preceding sequences that bind to a naturally occurring *patched* receptor, wherein the amount of the *hedgehog* polypeptide is effective to increase the rate of growth of the neuronal stem cells.

69. The method of any one of claims 1, 49, or 50, wherein said *hedgehog* protein is administered in combination with one or more other neurotrophic factors.

70. (Amended) The method of claim 69, wherein said other neurotrophic factor is selected from [the group consisting of] CNTF, BNTF, and NGF.

76. The method of claim 1, wherein said neuronal cells are neural progenitor cells.

H7

77. (Amended) The method of claim 1, wherein said neuronal cells differentiates into cells having a [particular] selected neural phenotype[, such as a neuron or a glia].

78. The method of claim 1, wherein said neuronal cells are in the central nervous system or the peripheral nervous system.

79. The method of claim 78, wherein said *hedgehog* treatment repairs central or peripheral nerve damage.

80. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide mimics the effect of a naturally [-] occurring *hedgehog* protein on one or more of growth, differentiation, and survival of neuronal cells.

82. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide comprises an amino acid sequence identical with all or a portion of an amino acid sequence designated in one of SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, [or] and SEQ ID NO: 34.

83. (Amended) The method of any one of claims 1, 49, or 50, wherein said *hedgehog* polypeptide has an amino acid sequence which is encoded by a nucleic acid which hybridizes under highly stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence selected from [the group consisting of] SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6 and SEQ ID NO: 7.

84. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide is encoded by a nucleic acid which is at least [80] 98% identical with all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, and [or] SEQ ID NO: 7.

85. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide is encoded by a nucleic acid which is at least 90% identical with all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, and [or] SEQ ID NO: 7.

86. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide is encoded by a nucleic acid which is at least 95% identical with all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, and [or] SEQ ID NO: 7.

93. (Amended) The method of any one of claim 1 [or 83], wherein said polypeptide includes a *hedgehog* amino acid sequence at least 80 percent identical with a sequence selected from [the group consisting of] residues 104-189 of SEQ ID NO: 8, residues 102-187 of SEQ ID NO: 9, residues 31-116 of SEQ ID NO: 10, residues 102-187 of SEQ ID NO: 11, or residues 101-186 of SEQ ID NO: 12.

94. (Amended) The method of claim 1, wherein said polypeptide includes a *hedgehog* amino acid sequence at least [70] 90 percent identical with a sequence selected from [the group consisting of] residues 27-189 of SEQ ID NO: 8, residues 22-187 of SEQ ID NO: 9, residues 1-116 of SEQ ID NO: 10, residues 25-187 of SEQ ID NO: 11, or residues 24-186 of SEQ ID NO: 12.

95. (Amended) The method of claim 1, wherein said polypeptide includes a *hedgehog* amino acid sequence at least [60] 90 percent identical with an amino acid sequence selected from [the group consisting of] residues 27-425 of SEQ ID NO: 8, residues 22-396 of SEQ ID NO: 9, residues 1-336 of SEQ ID NO: 10, residues 25-437 of SEQ ID NO: 11, residues 24-418 of SEQ ID NO: 12, or residues 24-475 of SEQ ID NO: 13, residues 1-312 of SEQ ID NO: 14.

96. The method of claim 1, wherein said polypeptide includes an amino acid sequence encoded by a naturally occurring vertebrate *hedgehog* gene.

97. The method of claim 96, wherein said *hedgehog* gene is a mammalian *hedgehog* gene.

98. The method of claim 97, wherein said *hedgehog* gene is a human *hedgehog* gene.

99. (Amended) The method of claim 1, wherein said polypeptide includes an amino acid sequence which is encoded by at least a portion of a *hedgehog* gene of vertebrate origin [corresponding to] selected from residues 64-567 of SEQ ID NO: 1, residues 64-561 of SEQ ID NO: 2, residues 1-348 of SEQ ID NO: 3, residues 73-561 of SEQ ID NO: 4, and residues 70-558 of SEQ ID NO: 5.

100. The method of claim 1, wherein said amino acid sequence is represented in the general formula SEQ ID NO: 41.

102. The method of claim 1, wherein said polypeptide includes at least 150 amino acid residues of the N-terminal half of a *hedgehog* protein.

103. The method of claim 1, wherein said polypeptide binds to a naturally occurring *patched* receptor.

104. The method of claim 103, wherein said *patched* receptor is a patched receptor of a vertebrate organism

107. (Amended) The method of claim 1, wherein said neuronal cells are selected from [the group consisting of] motor neurons, cholinergic neurons, dopaminergic neurons, [serotenergic] serotonergic neurons and peptidergic neurons.

108. The method of claim 1, wherein said *hedgehog* amino acid sequence is represented in the general formula SEQ ID NO: 40.

109. The method of claim 1, wherein said polypeptide includes at least 50 amino acid residues of the N-terminal half of a *hedgehog* protein.

110. The method of claim 1, wherein said polypeptide includes at least 100 amino acid residues of the N-terminal half of a *hedgehog* protein.

Please add the following new claims:

111. (New) A method for promoting one or more of growth, differentiation, and survival of neuronal cells, comprising contacting said cells with an [effective] amount of a *hedgehog* polypeptide encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19, or a fragment thereof that binds to a naturally occurring *patched* receptor, effective to promote one or more of growth, differentiation, and survival of said cells.

H8

112. (New) A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells with an effective amount of a *hedgehog* polypeptide encodable by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19, or a fragment thereof that binds to a naturally occurring *patched* receptor, thereby increasing the rate of survival of the neuronal cells.

113. (New) A method for promoting growth of mammalian neuronal stem cells, comprising treating the cells with an amount of a *hedgehog* polypeptide encoded by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19, or a

fragment thereof that binds to a naturally occurring *patched* receptor, effective to increase the rate of growth of the neuronal stem cells.

114.
~~113.~~ (New) The method of claim 50, wherein said polypeptide sequence comprises a polypeptide encoded by a nucleic acid which is at least 90% identical to all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19.

Rule 1.126

115.
~~114.~~ (New) The method of claim 50, wherein said polypeptide sequence comprises a polypeptide encoded by a nucleic acid which is at least 95% identical to all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2 SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19.

cont

116.
~~115.~~ (New) The method of claim 50, wherein said polypeptide sequence comprises a polypeptide encoded by a nucleic acid which is at least 98% identical to all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19.

H8

117.
~~116.~~ (New) The method of claim 49, wherein said polypeptide sequence comprises a polypeptide encoded by a nucleic acid which is at least 90% identical to all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19.

118.
~~117.~~ (New) The method of claim 49, wherein said polypeptide sequence comprises a polypeptide encoded by a nucleic acid which is at least 95% identical to all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2 SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19.

119
~~118.~~ (New) The method of claim 49, wherein said polypeptide sequence comprises a polypeptide encoded by a nucleic acid which is at least 98% identical to all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, or SEQ ID No: 19.

Rule 1.126

120. ~~119.~~ (New) The method of claim 1, wherein the N-terminal fragment is approximately 19 kD.

CNE

121. ~~119.~~ (New) The method of claim 49, wherein the N-terminal fragment is approximately 19 kD.

H8

122. ~~119.~~ (New) The method of claim 50, wherein the N-terminal fragment is approximately 19 kD.

The claims presented above incorporate changes as indicated by the marked-up versions below.

1. (Amended) A method for promoting one or more of growth, differentiation, and survival of neuronal cells, comprising contacting said cells with an [effective] amount of a *hedgehog* polypeptide at least 80% identical to a sequence selected from SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID No: 20, SEQ ID NO: 21 and N-terminal fragments of the preceding sequences that bind to a naturally occurring *patched* receptor, wherein the amount of the *hedgehog* polypeptide is effective to promote one or more of growth, differentiation, and survival of said cells.

49. (Amended) A method for promoting survival of mammalian neuronal cells responsive to *hedgehog* induction, comprising treating the cells with an effective amount of a *hedgehog* polypeptide at least 80% identical to a sequence selected from SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID No: 20, SEQ ID NO: 21 and N-terminal fragments of the preceding sequences that bind to a naturally occurring *patched* receptor, thereby increasing the [rate of] survival rate of the neuronal cells.

50. (Amended) A method for promoting growth of mammalian neuronal stem cells, comprising treating the cells with an [effective] amount of a *hedgehog* polypeptide at least 80%

identical to a sequence selected from SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID No: 20, SEQ ID NO: 21 and N-terminal fragments of the preceding sequences that bind to a naturally occurring *patched* receptor, wherein the amount of the *hedgehog* polypeptide is effective to increase the rate of growth of the neuronal stem cells.

70. (Amended) The method of claim 69, wherein said other neurotrophic factor is selected from [the group consisting of] CNTF, BNTF, and NGF.

77. (Amended) The method of claim 1, wherein said neuronal cells differentiates into cells having a [particular] selected neural phenotype[, such as a neuron or a glia].

80. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide mimics the effect of a naturally [-] occurring *hedgehog* protein on one or more of growth, differentiation, and survival of neuronal cells.

82. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide comprises an amino acid sequence identical with all or a portion of an amino acid sequence designated in one of SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, [or] and SEQ ID NO: 34.

83. (Amended) The method of any one of claims 1, 49, or 50, wherein said *hedgehog* polypeptide has an amino acid sequence which is encoded by a nucleic acid which hybridizes under highly stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence selected from [the group consisting of] SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6 and SEQ ID NO: 7.

84. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide is encoded by a nucleic acid which is at least [80] 98% identical with all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, and [or] SEQ ID NO: 7.

85. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide is encoded by a nucleic acid which is at least 90% identical with all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, and [or] SEQ ID NO: 7.

86. (Amended) The method of claim 1, wherein said *hedgehog* polypeptide is encoded by a nucleic acid which is at least 95% identical with all or a portion of a nucleic acid sequence designated in one of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, and [or] SEQ ID NO: 7.

93. (Amended) The method of any one of claim 1 [or 83], wherein said polypeptide includes a *hedgehog* amino acid sequence at least 80 percent identical with a sequence selected from [the group consisting of] residues 104-189 of SEQ ID NO: 8, residues 102-187 of SEQ ID NO: 9, residues 31-116 of SEQ ID NO: 10, residues 102-187 of SEQ ID NO: 11, or residues 101-186 of SEQ ID NO: 12.

94. (Amended) The method of claim 1, wherein said polypeptide includes a *hedgehog* amino acid sequence at least [70] 90 percent identical with a sequence selected from [the group consisting of] residues 27-189 of SEQ ID NO: 8, residues 22-187 of SEQ ID NO: 9, residues 1-116 of SEQ ID NO: 10, residues 25-187 of SEQ ID NO: 11, or residues 24-186 of SEQ ID NO: 12.

95. (Amended) The method of claim 1, wherein said polypeptide includes a *hedgehog* amino acid sequence at least [60] 90 percent identical with an amino acid sequence selected from [the group consisting of] residues 27-425 of SEQ ID NO: 8, residues 22-396 of SEQ ID NO: 9, residues 1-336 of SEQ ID NO: 10, residues 25-437 of SEQ ID NO: 11, residues 24-418 of SEQ ID NO: 12, or residues 24-475 of SEQ ID NO: 13, residues 1-312 of SEQ ID NO: 14.

99. (Amended) The method of claim 1, wherein said polypeptide includes an amino acid sequence which is encoded by at least a portion of a *hedgehog* gene of vertebrate origin [corresponding to] selected from residues 64-567 of SEQ ID NO: 1, residues 64-561 of SEQ ID